IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 10/502,140 Confirmation No. 9176
Applicants : Jung Joon Lee et al.
Filed : July 19, 2004
TC/A.U. : 1614
Examiner : McCormick Ewoldt, Susan Beth

Docket No. : 04-417
Customer No. : 34704

DECLARATION UNDER 37 C.F.R. §1.132

Mailstop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313

Dear Sir:

I, Jung Joon Lee, declare as follows:

1. I am a co-inventor of the present application.

2. I have read and understand and am familiar with U.S. Patent No. 6,365,768 to Palladino et al. and U.S. Patent No. 5,900,434 to Pyun et al.

3. I have read the claims of the present application as submitted in the response dated May 1, 2006.

4. I have conducted experiments to establish that a water extract taken from either the root or stem of *Acanthopanax Koreanum* as recited in claims 1-10 does not contain acanthoic acid. For purposes of comparison, I have also conducted experiments to establish that an ethanol extract taken from either the root or stem of *Acanthopanax Koreanum* does contain acanthoic acid.

5. The preparation of a water extract from the root of *Acanthopanax Koreanum* (Sample 1) was conducted as follows: A root of *Acanthopanax Koreanum* was dried and sliced into small pieces. A 10-L round-bottomed flask was charged with 1 kg of sliced root and a quantity of water. The sliced root and water were mixed and extracted at a temperature of greater than 90°C for 3 hours. The extraction was repeated two times. The extracted solution was filtered through filtrate membranes, concentrated under a reduced pressure in a rotary evaporator, and lyophilized to yield a water extract from the root of *Acanthopanax Koreanum* weighing 142 g.

6. The preparation of an ethanol extract from the root of the *Acanthopanax Koreanum* (Sample 2) was conducted as follows: The root of *Acanthopanax Koreanum* was dried and sliced into small pieces. A 2-L round-bottomed flask fitted with a reflux condenser was charged with 0.1 kg of sliced root and 500 mL of ethanol. The sliced root and ethanol were mixed, heated at a temperature of 80°C for 5 hours using a heating mantle, and extracted. The extracted solution was filtered through filtrate membranes, concentrated using a rotary evaporator, and dried under a reduced pressure in a vacuum oven to yield an ethanol extract from the root of *Acanthopanax Koreanum* weighing 5 g.

7. The preparation of a water extract from the stem of the *Acanthopanax Koreanum* (Sample 3) was conducted as follows: The stem of *Acanthopanax Koreanum* was dried and sliced into small pieces. A 10-L round-bottomed flask was charged with 1 kg of sliced root and a quantity of water. The sliced root and water were mixed and extracted at a temperature of greater than 90°C for 3 hours. The extraction was repeated two times. The extracted solution was filtered through filtrate membranes and concentrated under reduced pressure in a rotary evaporator, and lyophilized to yield a water extract from the stem of *Acanthopanax Koreanum* weighing 80 g.

8. The preparation of an ethanol extract from the stem of *Acanthopanax Koreanum* (Sample 4) was conducted as follows: The stem of *Acanthopanax Koreanum* was dried and sliced into small pieces. A 2-L round-bottomed flask fitted with a reflex condenser was charged with 0.1 kg of sliced root and a 500 mL of ethanol. The sliced root and ethanol were mixed, heated at a temperature of 80°C for 5 hours using a heating mantle, and extracted. The extracted solution was filtered through filtrate membranes, concentrated using a rotary evaporator, and dried under reduced pressure in a vacuum oven to yield an ethanol extract from the stem of *Acanthopanax Koreanum* weighing 3 g.

9. Each sample 1-4 was prepared for HPLC analysis using an HPLC commercially available from the Dionex Corporation of Sunnyvale, Canada. The HPLC was composed of a Dionex PDA Photodiode Array Detector, an ASI-100 Automated Sample Injector, a P580 pump, a J'sphere ODS-H80 Column (250mm x 4.6mm I.D.). The HPLC tests were conducted using sample injections measuring 20 μl, a solvent mixture of acetonitrile (ACN) and water 10% (volume/volume, ACN to water) to 100% (volume/volume, ACN to water) gradient, 60 min. The flow rate was 1 ml/min., and the detection wavelength was 207 nm.

10. The HPLC test of sample 1 was conducted as follows: A portion of sample 1 was solubilized in pure methanol, for final concentration of analyzed sample 1 to be 1 mg/ml. An HPLC chromatogram of sample 1 is shown in Exhibit A attached hereto.

11. The HPLC test of sample 2 was conducted as follows: A portion of sample 2 was solubilized in pure methanol, for final concentration of analyzed sample 2 to be 1 mg/ml. An HPLC chromatogram of sample 2 is shown in Exhibit A attached hereto.

12. The HPLC test of sample 3 was conducted as follows: A portion of sample 3 was solubilized in pure methanol, for final concentration of analyzed sample 3 to be 1 mg/ml. An HPLC chromatogram of sample 3 is shown in Exhibit B attached hereto.

13. The HPLC test of sample 4 was conducted as follows: A portion of sample 4 was solubilized in pure methanol, for final concentration of analyzed sample 4 to be 1

mg/ml. An HPLC chromatogram of sample 4 is shown in Exhibit B attached hereto.

14. I also prepared six standard solutions of several compounds (of Exhibit C attached hereto) identified as "EE" (Table 1), "EB" (Table 2), "TA" (Table 3), "Sy" (Table 4), "AA" (Table 5), and "KA" (Table 6) for quantitative analysis. Each standard solution was prepared for final concentration shown in Tables 1-6, respectively. Each standard solution underwent HPLC testing. The HPLC analysis of each standard solution was accomplished and the concentration-area was plotted as a standard curve of Tables 1-6 attached hereto. The standard curve was used to measure the quantity of the content of each standard solution.

15. The HPLC results of the water extracts from both the root and stem of *Acanthopanax Koreanum* shown in Exhibits A and B demonstrate the absence of acanthoic acid.

16. The HPLC results of the ethanol extracts from both the root and stem of *Acanthopanax Koreanum* shown in Exhibits A and B demonstrate the presence of acanthoic acid.

17. The disclosure of U.S. Patent No. 6,365,768 to Palladino et al. teaches extracting and isolating acanthoic acid, at least in the form of a crude extract containing acanthoic acid, from the root bark of *Acanthopanax koreanum* Nakai.

18. The disclosure of U.S. Patent No. 6,365,768 to Palladino et al. teaches the extract of paragraph 17 may produced according to the following method: dried root bark of *Acanthopanax koreanum* Nakai chipped and covered with 1L to 3L of a suitable solvent, most preferably methanol (col. 20, l. 66-col. 21, l. 10).

19. The methanol extract from the root bark of *Acanthopanax koreanum* Nakai taught by Palladino contains acanthoic acid, while the experiments set forth herein that I conducted demonstrate that water extracts from the both the root and stem of *Acanthopanax koreanum* shown in Exhibits A and B do not contain acanthoic acid.

20. The disclosure of U.S. Patent No. 5,900,434 to Pyun et al. teaches extracting and isolating acanthoic acid from the dried root bark of *Acanthopanax koreanum* Nakai.

21. The disclosure of U.S. Patent No. 5,900,434 to Pyun et al. teaches the extract of paragraph 20 may be produced adding 1 kg of dried root bark to 1L to 3L of methanol (or diethyl ether or mixture thereof) (col. 3, l. 49-col. 4, l. 3).

22. The methanol extract from the root bark of *Acanthopanax koreanum* Nakai taught by Pyun contains acanthoic acid, while the experiments set forth herein that I conducted demonstrate that water extracts from the both the root and stem of *Acanthopanax koreanum* shown in Exhibits A and B do not contain acanthoic acid.

23. These experiments set forth herein that I conducted demonstrate the methanol extracts taught by both Palladino and Pyun do not contain all of the characteristics claimed in claims 1-10 of the present application.

24. The results of these experiments demonstrate conclusively the Palladino reference does not anticipate claims 1-10 of the present application.

25. The results of these experiments also demonstrate conclusively the Pyun reference does not anticipate claims 1-10 of the present application.

26. These experiments set forth herein that I conducted establish that an unobvious difference exists between the subject matter of claims 1-10 of the present application and the teachings of both Palladino and Pyun.

27. The results of these experiments demonstrate conclusively claims 1-10 of the present application are patentable over the Palladino reference.

28. The results of these experiments also demonstrate conclusively claims 1-10 of the present application are patentable over the Pyun reference.

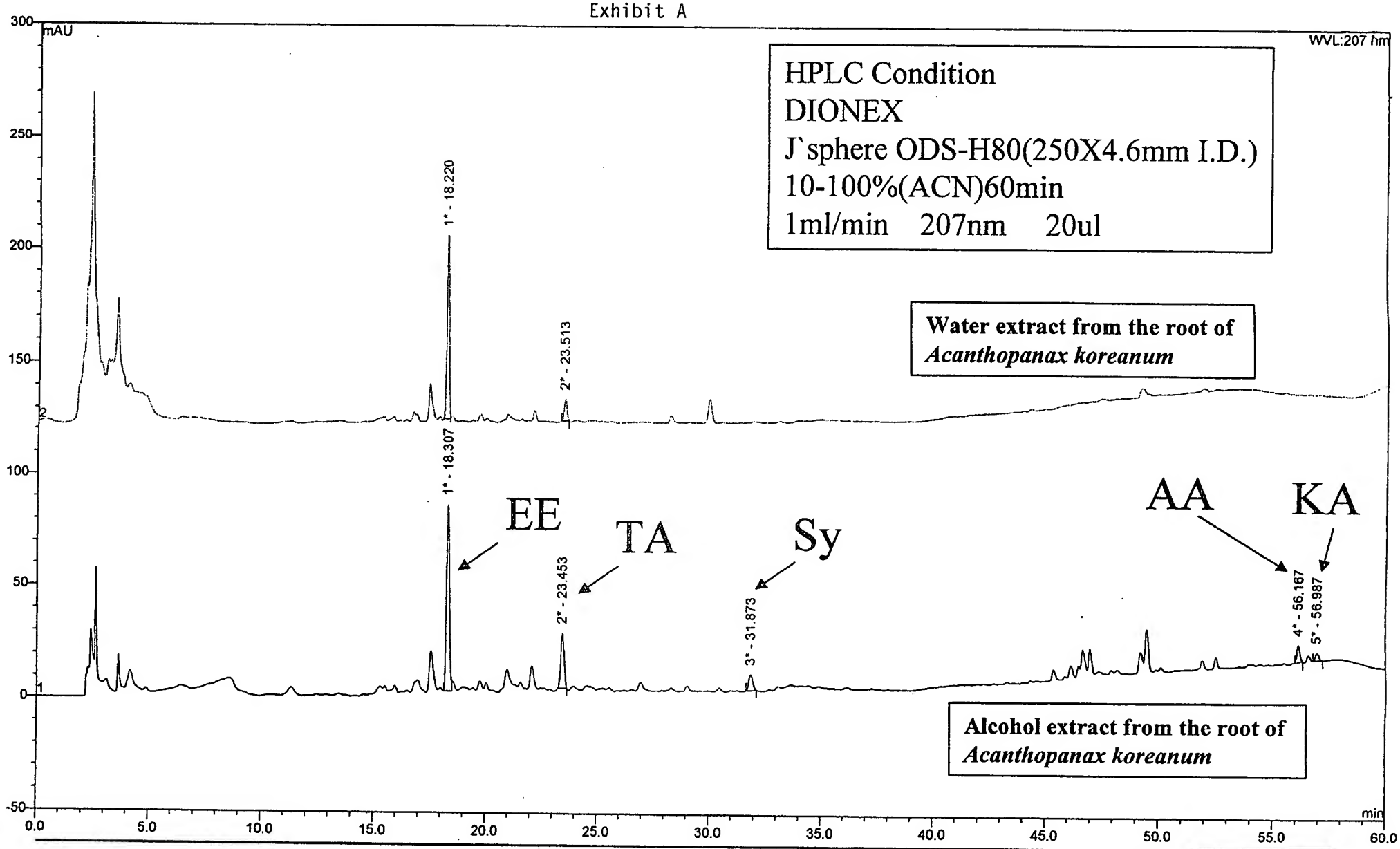
29. The undersigned declares further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Respectfully submitted,

Lee, Jung Joon

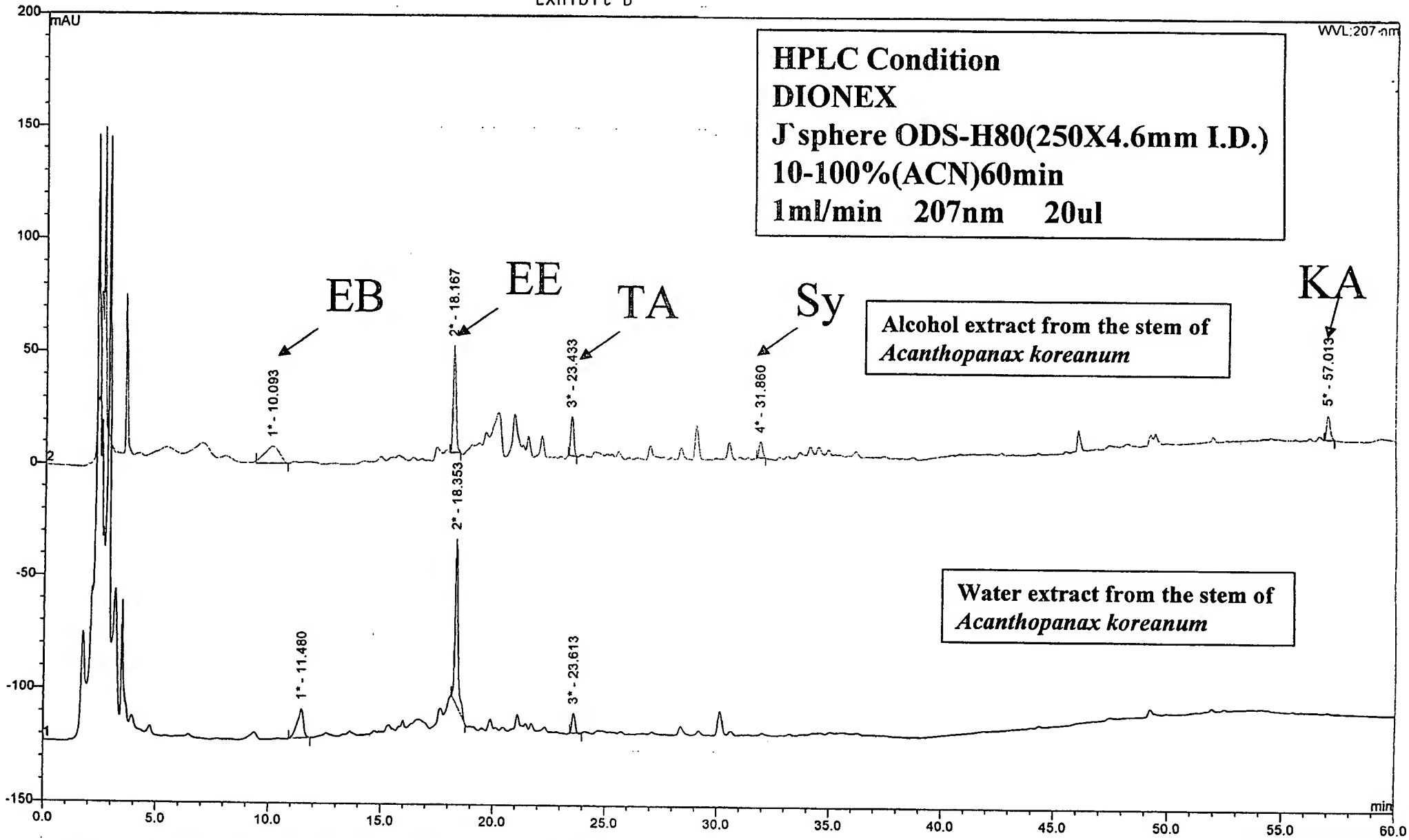
Jung Joon Lee
Dated: January 8, 2007

Exhibit A



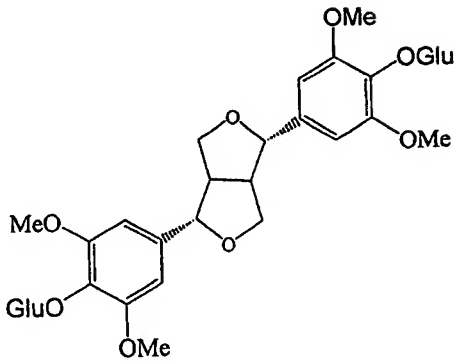
%/ext wt	EE	TA	Sy	EB	AA	KA
Alcohol extract from the root of *Acanthopanax koreanum*	0.72	0.37	0.13	–	0.83	0.57
Water extract from the root of *Acanthopanax koreanum*	0.58	0.12	–	–	–	–

Exhibit B



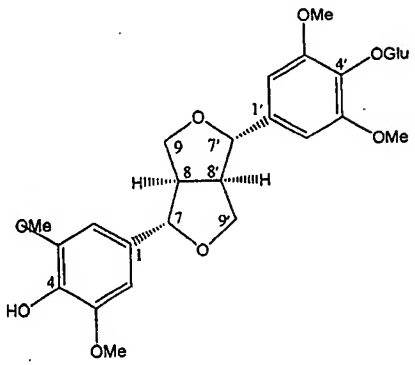
%/ext wt	EE	TA	Sy	EB	AA	KA
Alcohol extract from the stem of *Acanthopanax koreanum*	0.45	0.24	0.12	0.44	–	1.54
Water extract from the stem of *Acanthopanax koreanum*	0.65	0.11	–	0.35	–	–

Exhibit C



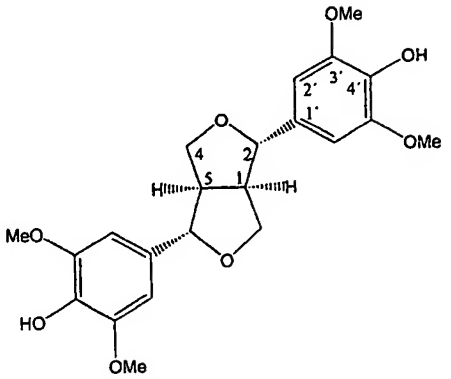
EE

Eleutheroside E



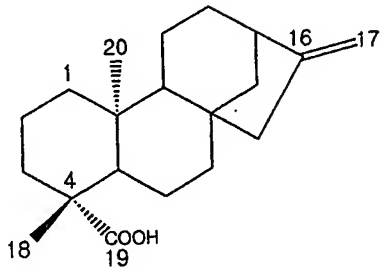
TA

Tortoside A



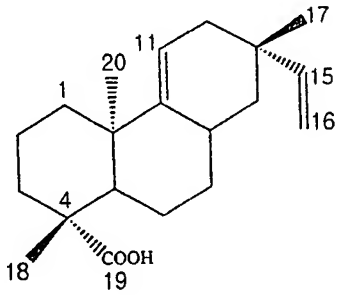
Sy

(+)-Syringaresinol



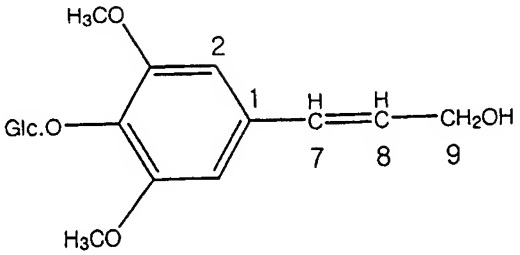
KA

Ent-kaur-16-en-19-oic acid



AA

Acanthoic acid



EB

Eleutheroside B

Concentration of standard solution(ug/ml)	Area
5	10.40
25	48.20
50	109.53

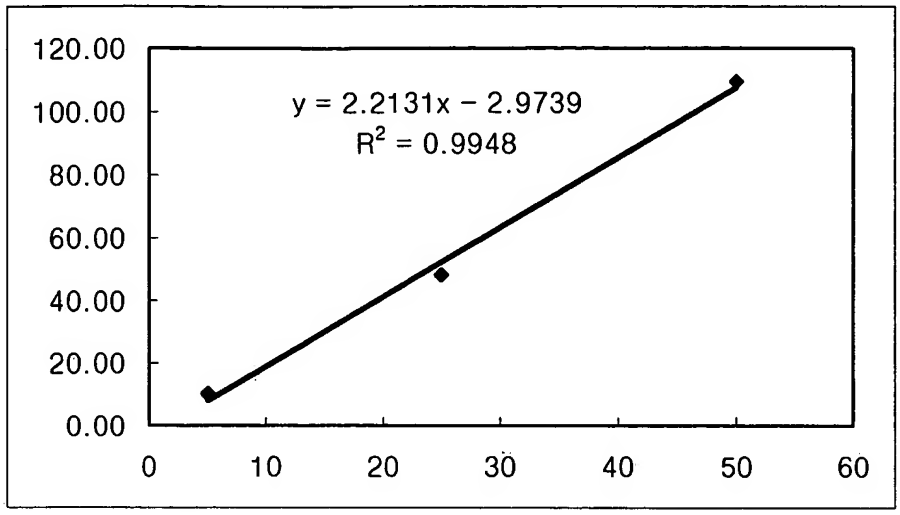


Table 1

Concentration of standard solution(ug/ml)	Area
1	1.41
5	5.75
25	29.07

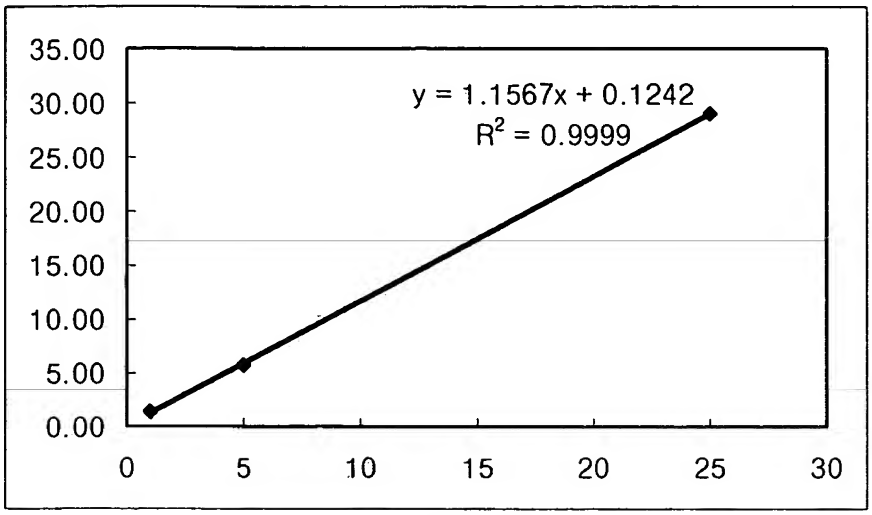


Table 2

Tortoside A Content 6.21.2006

Concentration of standard solution (ug/ml)	Area
1	1.13
5	5.73
25	27.13

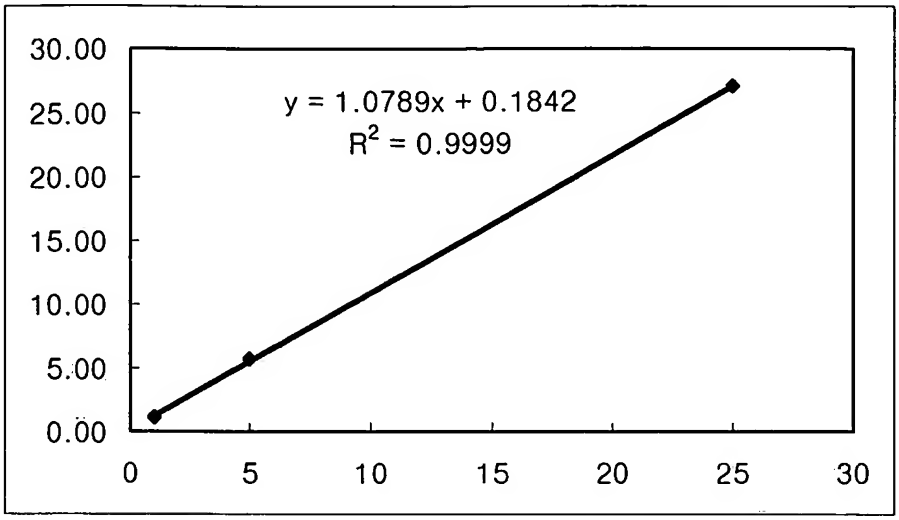


Table 3

Concentration of standard solution (ug/ml)	Area
1	1.30
5	6.10
25	33.80

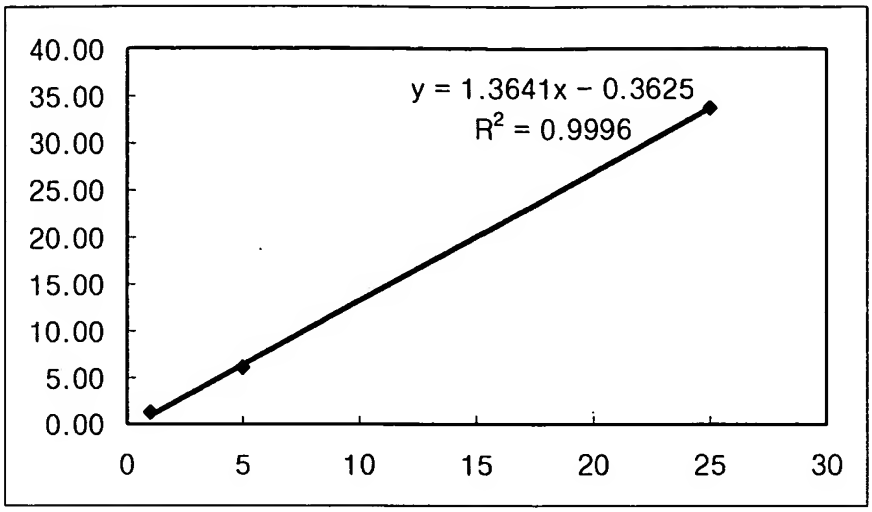


Table 4

Concentration of standard solution (ug/ml)	Area
5	0.66
25	3.64
50	7.50

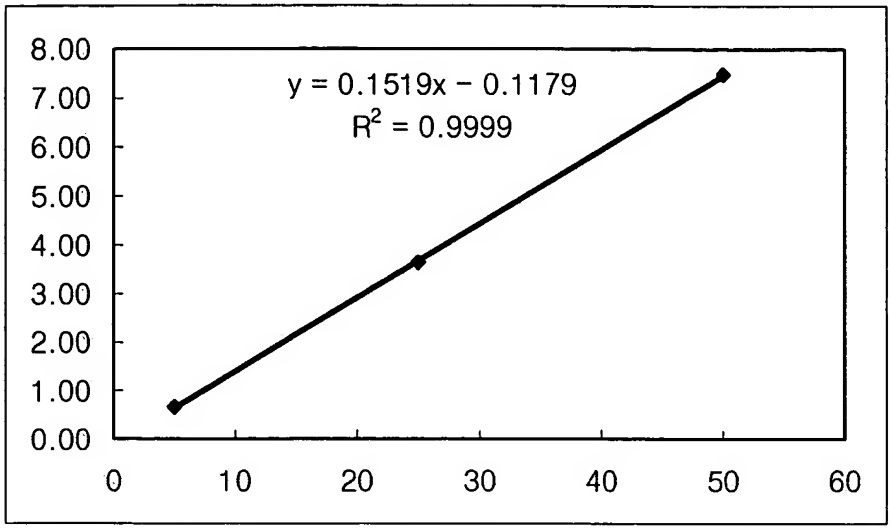


Table 5

Concentration of standard solution (ug/ml)	Area
5	0.60
25	3.45
50	7.57

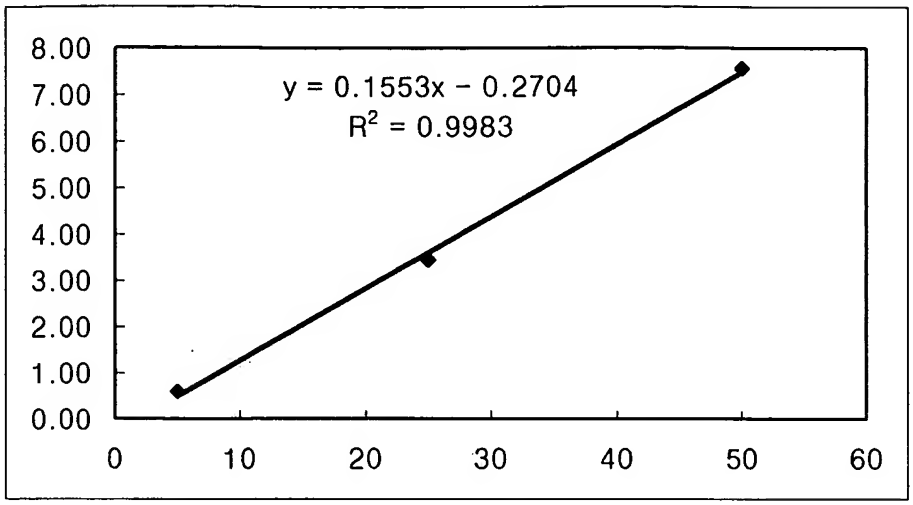


Table 6